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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/552,206

09/14/2006

Irina Velikyan

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EXAMINER

PERREIRA, MELISSA JEAN

ART UNIT

PAPER NUMBER

1618

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/552,206	<b>Applicant(s)</b> VELIKYAN ET AL	
	<b>Examiner</b> MELISSA PERREIRA	<b>Art Unit</b> 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 August 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/18/08 has been entered.

### ***Claims and Previous Rejection Status***

2. Claims 1-19 are pending in the application.
3. The rejection of claims 1-19 under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (WO03/059397A2) in view of Bottcher et al. (US 5,439,863) and further in view of Maier-Borst et al. (GB 2056471A) is maintained.
4. The provisional rejection of claims 8-12 and 14 under 35 U.S.C. 101 as claiming the same invention as that of claims 1,3-7,11,13,15 of copending Application No. 10/552,134 is maintained.
5. The provisional rejection of claims 1,2,6-14 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of copending Application No. 11/358,681 is maintained.

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6. The provisional rejection of claims 1-14 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of copending Application No. 10/552,134 is maintained.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (WO03/059397A2) in view of Bottcher et al. (US 5,439,863) and further in view of Maier-Borst et al. (GB 2056471A).

9. Griffiths et al. (WO03/059397A2) discloses the method of producing a  $^{68}\text{Ga}$ -radiolabeled complex/ $^{68}\text{Ga}$ -labeled targeting agent for use in PET detection (p4, paragraph 2; p9, paragraph 1). The method of obtaining the  $^{68}\text{Ga}$  involves eluting  $^{68}\text{Ga}$  from a  $^{68}\text{Ge}/^{68}\text{Ga}$  titanium dioxide based in-house generator. The  $^{68}\text{Ga}$  is eluted from the titanium dioxide generator, which can be fitted with an anion-exchange membrane/Q5F cartridge (p14, paragraph 1) with acidic solution, such as 0.5-1N HCl (p7, paragraph 3; p8, paragraph 2; p12, paragraph 1). The method of producing a radiolabeled gallium complex involves reacting the solution of a peptide labeled macrocyclic chelate with the  $^{68}\text{Ga}$  diluted from the  $^{68}\text{Ge}/^{68}\text{Ga}$  titanium dioxide generator (p14, paragraph 1). The chelate-targeting agent conjugates can be compounded into

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kits that are ready to use and accept the  $^{68}\text{Ga}$  elute (p8, paragraph 3). The macrocyclic-chelating agent, such as DOTA or NOTA may be linked to a peptide that can target the site of a disease, thus generating a bifunctional chelating agent comprising a targeting vector which will be site-specific (p9, paragraph 1; p11, paragraphs 1 and 2). Griffiths et al. does not disclose the preparation of the chelate-targeting agent conjugates via microwave acceleration. Griffiths et al. also does not disclose an anion exchanger comprising  $\text{HCO}_3^-$  or more specifically one comprising an amine functional groups or one based on polystyrene-divinylbenzene.

10. Bottcher et al. (US 5,439,863) discloses the preparation of metal complex salts via microwave irradiation (column 3, line 44-46). The complexes are prepared from metal ions, such as those of the second and third main group, not excluding gallium and multitoothed chelating ligands that occupy more than one coordination site on the central metal atom (column 3, lines 55-59; column 4, lines 44-46). The ligands of the disclosure may include those with dioxime (N and O containing), etc. groups (column 5, lines 20-24). The use of microwave as the high-energy input allows for a continuous conversion, single-stage reaction with short reaction time and ease of separation of the formed complexes (column 4, line 19; column 5, lines 66+; column 6, lines 1-5).

11. Maier-Borst et al. (GB 2056471A) discloses the separation of  $^{68}\text{Ga}$  for its parent nuclide, germanium-68, with water via passing the eluant from a generator column into an anion exchanger comprising quaternary ammonium groups incorporated in a matrix of styrene and divinylbenzene and washing the anion exchanger with water (p4, lines 44-48).

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12. At the time of the invention it would have been obvious to produce a  $^{68}\text{Ga}$ -DOTA-peptide complex for use as a PET tracer via the production of  $^{68}\text{Ga}$  from a  $^{68}\text{Ge}/^{68}\text{Ga}$  titanium dioxide generator as disclosed by Griffiths et al. The microwave synthesis technique for the method of producing metal-chelate complexes was known by Bottcher et al. thus, it would have been obvious to utilize (try) the microwave acceleration technique for a faster, more reproducible preparation of the  $^{68}\text{Ga}$ -DOTA-peptide complex, such as that of Griffiths et al. to generate a complex useful in the treatment or diagnosis of tumours with minimal side product formation. Microwave acceleration techniques have been utilized since the 1980's in a number of production methods for radioactive precursors and radiotracers labeled with positron-emitting nuclides. The microwave method is mostly associated with shortened reaction times and encompasses the microwave conditions of the instant claims. Since the microwave technique was known in the art (Bottcher et al.) one would have a reasonable expectation of success for preparing radiotracer via labeling reactions with this improved microwave technique.

13. It would have been obvious to utilize (try) an anion exchanger of Maier-Borst et al. to separate  $^{68}\text{Ga}$  from its parent nuclide since no chelating agent is required for separation and as Maier-Borst et al. is drawn to the same method of separation as the instant claims. It is known in the art to add a chelating agent, such as EDTA to elute  $^{68}\text{Ga}$  from an aluminum oxide exchanger. The disadvantage of forming the  $^{68}\text{Ga}$ -EDTA complex is that the complex has to be destroyed before further processing to obtain

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radiopharmaceutical agents which is time-consuming and expensive (see Maier-Borst et al. p1, lines 10-16).

### ***Double Patenting***

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 8-12 and 14 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1,3-7,11,13,15 of copending Application No. 10/552,134. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

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from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1,2,6-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of copending Application No. 11/358,681. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method for producing a <sup>68</sup>Ga-radiolabelled complex of the instant claims encompasses the method for labeling synthesis of radiolabeled gallium complex of 11/358,681. The method of the instant claims includes the method of obtaining <sup>68</sup>Ga by contacting the eluate from a <sup>68</sup>Ge/<sup>68</sup>Ga generator which is also disclosed in the method of 11/358,681. The macrocyclic chelating agents (DOTA), the generator column (titanium dioxide), the strong anion exchangers and the use of microwave activation for the preparation are identical for the instant claims and copending Application No. 11/358,681. The species of targeting vector protein, such as hEGF of 11/358,681 anticipate the genus of targeting vector proteins of the instant claims. Therefore, the resulting radiolabeled gallium complex of



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the instant claims is obviously generated and isolated via the synthesis and would encompass that radiolabeled gallium complex of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of copending Application No. 10/552,134. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of producing a  $^{68}\text{Ga}$ -radiolabeled complex of the instant claims encompasses the method of producing a radiolabeled gallium complex of the copending Application No. 10/552,134 since the method steps are identical. Both inventions involve reacting a  $^{68}\text{Ga}$  radioisotope with a macrocyclic or bifunctional chelating agent via microwave. The inventions also include a targeting moiety that may be bound to the chelating agent for site-directed localization. The generation of the  $^{68}\text{Ga}$  radioisotope of both applications involves eluting the  $^{68}\text{Ga}$  from a  $^{68}\text{Ge}/^{68}\text{Ga}$  titanium dioxide generator followed by purification of the  $^{68}\text{Ga}$  eluate via a strong anion exchanger. Therefore, the resulting radiolabeled gallium complex of the instant claims is obviously generated via the synthesis and isolated and would encompass that radiolabeled gallium complex of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Response to Arguments***

14. Applicant's arguments filed 8/18/08 have been fully considered but they are not persuasive.

15. Applicant asserts that Bottcher et al. does not discuss how microwave technology could be used as an input of energy and does not deem these inputs of energy as important parts of its patent.

16. The reference of Bottcher et al. is a patent and therefore contains an enabling disclosure. The limitation of using microwaves to form the complexes does not need to be exemplified and the assertion that Bottcher et al. does not deem microwave as an important part of its patent is merely the opinion of the applicant.

17. Applicant asserts that Bottcher et al. does not teach microwaves are preferred over using ultrasound or laser beams as inputs of energy.

18. The limitation of using microwaves to form the complexes does not need to be exemplified and it would be obvious to utilize or try any of the inputs of energy disclosed as it would be predictable that any of the inputs of energy, such as microwave allows for a continuous conversion, single-stage reaction with short reaction time and ease of separation of the formed complexes (column 4, line 19; column 5, lines 66+; column 6, lines 1-5).

19. Applicant asserts that Bottcher et al. does not disclose, teach or suggest using a microwave oven as disclosed in the present invention to enhance or improve efficiency and reproducibility of the neutral metal complex salt formation.

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20. The instant claims do not recite a "microwave oven" but recites, "the reaction is carried out using microwave activation" and the microwave energy of Bottcher et al. encompasses the microwave activation of the instant claims and is capable of the same functions, such as enhance or improve efficiency and reproducibility of the neutral metal complex salt formation.

21. Applicant asserts that if Bottcher et al. used the same microwave technology, such as a microwave oven, utilized in the present invention then Bottcher et al. would have found that the use of microwave activation substantially improves the efficiency and reproducibility of its neutral metal complex salt formation.

22. Bottcher et al. does teach that the formation of the complexes themselves will be accelerated (improved efficiency) through high energy input or through the effect of microwaves (column 3, lines 38-45). The limitation of using microwave energy to form the complexes does not need to be exemplified.

23. Applicant asserts that Bottcher et al. does not use the microwave activation technique disclosed in the present invention to carry out the coordination chemistry.

24. The limitation of using microwaves to form the complexes does not need to be exemplified and it would be obvious to utilize or try any of the inputs of energy disclosed to prepare the neutral metal complexes as it would be predictable that any of the inputs of energy, such as microwave allows for a continuous conversion, single-stage reaction with short reaction time and ease of separation of the formed complexes (column 4, line 19; column 5, lines 66+; column 6, lines 1-5).

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25. Applicant asserts that the objective of Maier-Borst et al. was to synthesize an anion exchange resin for the separation of gallium-68 from germanium-68 thus avoiding the use of EDTA for elution as it was done before the 1980's.

26. The instant claims are drawn to the method of obtaining  $^{68}\text{Ga}$  from a  $^{68}\text{Ge}/^{68}\text{Ga}$  generator with an anion exchanger, such as polystyrene-divinylbenzene and a dilute HCl solution. The reference of Maier-Borst et al. is drawn to process for preparing an ion (anion)-exchanger and further is drawn to the method of obtaining  $^{68}\text{Ga}$  from a  $^{68}\text{Ge}/^{68}\text{Ga}$  generator with the anion exchanger, such as styrene and divinylbenzene and a dilute HCl solution (p1, lines 59-63) and therefore the method of Maier-Borst et al. encompasses the method of the instant claims and is capable of the same functions (i.e. labeling efficiency, etc.) and has the same properties. Also, the instant claims do not provide the limitations of a preconcentration procedure which is asserted as necessary by the applicant.

27. Applicant asserts that the claims of copending application 10/552,134 will be amended or cancelled if the instant application is indicated to be allowable.

28. The rejection is maintained as the claims have not been amended and the copending application 10/552,134 has not been abandoned.

29. Applicant asserts that a terminal disclaimer will be filed for applications 11/358,681 and 10/552,134 once the instant application is indicated as allowable.

30. The rejections are maintained as terminal disclaimers have not been filed.

***Conclusion***

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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